



RECEIVED

APR 11 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Kirk Hogan  
Serial No.: 09/613,887  
Filed: July 11, 2000  
Entitled:

Group No.: 1655  
Examiner: J.E. Goldberg

**Methods and Compositions for Perioperative Genomic Profiling**

**SUPPLEMENTAL INFORMATION DISCLOSURE  
STATEMENT TRANSMITTAL**

Assistant Commissioner for Patents  
Washington, D.C. 20231

<b>CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)</b>	
I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
Dated: <u>March 28, 2001</u>	By: <u>Mary Ellen Waite</u> Mary Ellen Waite

Sir or Madam:

Enclosed please find an Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

A check for \$180.00 is also enclosed pursuant to 37 C.F.R. § 1.17(p) for filing this Information Disclosure Statement after three months as set forth in 37 C.F.R. § 1.97(c).

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. 08-1290. **An originally executed duplicate of this transmittal is enclosed for this purpose.**

Dated: March 28, 2001

David A. Casimir  
Registration No. 42,395

04/09/2001 BNGUYEN1 00000013 09613887

01 FC:126

180.00-0P

MEDLEN & CARROLL, LLP  
220 Montgomery Street, Suite 2200  
San Francisco, California 94104  
415/705-8410



1655 #6  
PATENT  
Attorney Docket No. HOGAN-04448  
127

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Kirk Hogan

Serial No.: 09/613,887

Filed: July 11, 2000

Entitled: **Methods and Compositions for Perioperative Genomic Profiling**

Group No.: 1655

Examiner: J.E. Goldberg

**SUPPLEMENTAL INFORMATION  
DISCLOSURE STATEMENT**

RECEIVED

APR 11 2001

Assistant Commissioner for Patents  
Washington, D.C. 20231

TECH CENTER 1600/2900

**CERTIFICATE OF MAILING UNDER 37 CFR § 1.8(a)**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231, on **March 28, 2001**.

By: Mary Ellen Waite

Mary Ellen Waite

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

Applicant has become aware of the following printed publications which may be material to the examination of this application:

- Sweietzer B. (ed.), *Handbook of Preoperative Assessment and Management*, first edition, [2000], Lippincott, Williams and Wilkins, pgs 16-38.
- Erickson *et al.*, *Anesthesia and Perioperative Complications*, second edition, [1999] pp. 741-751, Assessment of Anesthetic Risk.
- Baum *et al.*, *Anesthesia for Genetic, Metabolic, and Dysmorphic Syndromes of Childhood*, first edition, [1999], Lippincott, Williams and Wilkins. This

reference is a textbook and is not being supplied at this time but will be supplied at the Examiner's request.

- Hardman *et al.*, *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, ninth edition, [1996], McGraw-Hill. This reference is a textbook and is not being supplied at this time but will be supplied at the Examiner's request.
- Bothner *et al.*, Building a large scale perioperative anaesthesia outcome-tracking database: methodology, implementation, and experiences from one provider within the German quality project. *British Journal of Anaesthesia* 85(2): 271-80, 2000.
- Douglas, Malignant hyperthermia persists though its profile changes. *Anesthesiology News* 25: 1 [1999]
- Savarese *et al.*, *Anesthesia* (RD, M., Ed.) pp 420, and 453, Churchill Livingstone, Philadelphia, PA. [2000]
- Jacobs, *Progress in Anes* 7:39 [1998]. This reference is not being supplied at this time but will be supplied when available.
- Schein *et al.*, *NEJM* 342:168 [2000]
- Roizen, *NEJM* 342:204 [2000]
- Prows *et al.*, Optimizing drug therapy based on genetic differences: implications for the clinical setting. *AACN Clinical Issues* 9(4), 499-512, 1998.
- Kalow, *Pharmacological Reviews* 49:369 [1997] Pharmacogenetics in biological perspective.
- Vesell, *Ann Int Med* 126:653 [1997] Therapeutic lessons from pharmacogenetics.
- Ball *et al.*, *Nature Biotechnology* 15:925 [1997] Pharmacogenetics and drug metabolism.
- Evans *et al.*, *Science* 286:487 [1999] Pharmacogenomics: translating functional genomics into rational therapeutics.
- Nebert, *Clin Genet* 56: 247 [1999] Pharmacogenetics and pharmacogenomics: why is this relevant to the clinical geneticist?

- Beaudet, *Am J Hum Genet* 64:1 [1999] 1998 ASHG presidential address.  
Making genomic medicine a reality.
- Nebert, *Am J Hum Genet* 60:265 [1997] Polymorphisms in drug-metabolizing enzymes: what is their clinical relevance and why do they exist?
- Daly, *J Mol Med* 73:539 [1995] Molecular basis of polymorphic drug metabolism.
- Dale *et al.*, *Acta Anaesthesiol Scand* 42:1025 [1998] Cytochrome P450, molecular biology and anaesthesia.
- Meyer, *PNAS* 91:1983 [1994] Pharmacogenetics: the slow, the rapid, and the ultrarapid.
- Brown *et al.*, *Nature Genetics* 18:91 [1998] Genomics and human disease--variations on variation.
- Marshall, *Nature Biotechnology* 15:954 [1997] Laying the foundations for personalized medicines.
- Time poll on genetic testing. [1999]
- Licking, The Great Chip Derby. *Business Week* 10/25/99, 90, [1999]
- Griffin *et al.*, *PNAS*, 96:6301 [1999] Direct genetic analysis by matrix-assisted laser desorption/ionization mass spectrometry.
- Yox, *Laboratory Medicine* 30: 456 [1999]
- Gunderson *et al.*, *Genome Research* 8: 1142 [1998] Mutation detection by ligation to complete n-mer DNA arrays.
- Harris *et al.*, *Nature Biotechnology* 18: 384 [2000] Injecting new ideas into microarray printing.
- Steemers *et al.*, *Nature Biotechnology* 18: 91 [2000] Screening unlabeled DNA targets with randomly ordered fiber-optic gene arrays.
- Chen *et al.*, *Genome Research* 10: 549 [2000] A microsphere-based assay for multiplexed single nucleotide polymorphism analysis using single base chain extension.
- Garvin *et al.*, *Nature Biotechnology* 18: 95 [2000] MALDI-TOF based mutation detection using tagged in vitro synthesized peptides.
- Griffin *et al.*, *TIBTECH* 18: 77 [2000]

- *Nature Genetics* 21:1 [1999] "The Chipping Forecast". This reference is not being supplied at this time but will be supplied when available.
- Fodor, *Science* 277: 393 [1997]
- Gerhold *et al.*, DNA chips: promising toys have become powerful tools. *TIBS* 24: (May) [1999]
- Blanchard *et al.*, *Nature Biotechnology* 17: 953 [1999] Cheap DNA arrays-it's not all smoke and mirrors.
- Gilles *et al.*, *Nature Biotechnology* 17: 365 [1999] Single nucleotide polymorphic discrimination by an electronic dot blot assay on semiconductor microchips.
- Sapolsky *et al.*, *Genetic Analysis* 14: 187 [1999] High-throughput polymorphism screening and genotyping with high-density oligonucleotide arrays.
- Drmanac *et al.*, *Nature Biotechnology* 16: 54 [1998] Accurate sequencing by hybridization for DNA diagnostics and individual genomics.
- Cotton, *Genetic Analysis* 14: 165 [1999] Mutation detection by chemical cleavage.
- Schafer *et al.*, *Nature Biotechnology* 16:33 [1998] DNA variation and the future of human genetics.
- Henke C. IVD Technology Magazine.  
<[www.devicelink.com/ivdt/archive/99/008.html](http://www.devicelink.com/ivdt/archive/99/008.html)> and < . . .  
archive/9i8/11/010.tml>, < . . . archive/99/01/008.html> [1998]
- Ryan *et al.*, *Molecular Diagnosis* 4: 135 [1999] Non-PCR-dependent detection of the factor V Leiden mutation from genomic DNA using a homogeneous invader microtiter plate assay. This reference is not being supplied at this time but will be supplied when available.
- Kaiser *et al.*, *J Biol Chem* 274: 21387 [1999] A comparison of eubacterial and archaeal structure-specific 5'-exonucleases.
- Oldenburg *et al.*, *BioTechniques* 28: 351 [2000] New Cleavase Fragment Length Polymorphism method improves the mutation detection assay.

- Andersen *et al.*, *Molecular Diagnosis* 3: 105 [1998] Mutation Detection by Cleavase in Combination With Capillary Electrophoresis Analysis: Application to Mutations Causing Hypertrophic Cardiomyopathy and Long-QT Syndrome. This reference is not being supplied at this time but will be supplied when available.
- Mein *et al.*, *Genome Research* 10: 330 [2000] Evaluation of single nucleotide polymorphism typing with invader on PCR amplicons and its automation.
- Issaksson IA *et al.*, *Curr Opin Biotechnol* 10: 11 [1999]
- Vaughan *et al.*, *Genetic Analysis* 14: 169 [1999] Glycosylase mediated polymorphism detection (GMPD)--a novel process for genetic analysis.
- Graves, *Trends Biotechnol* 17: 127 [1999] Powerful tools for genetic analysis come of age.
- Walt., *Science* 287:451 [2000] Techview: molecular biology. Bead-based fiber-optic arrays.
- Persidis, *Hospital Practice* 11/15/99: 67 [1999] Biochips: an evolving clinical technology.
- Taylor *et al.*, *Genetic Analysis* 14:181 [1999] Enzymatic methods for mutation scanning.
- Cargill *et al.*, *Nature Genetics* 22:231 [1999] Characterization of single-nucleotide polymorphisms in coding regions of human genes.
- Sleigh *et al.*, *Anaesth Intensive Care* 28: 54 [2000] Generic polymerase chain reaction followed by DNA sequencing as a means of diagnosing bacteraemia.
- Halushka *et al.*, *Nature Genetics* 22: 239 [1999] Patterns of single-nucleotide polymorphisms in candidate genes for blood-pressure homeostasis.
- Kwok, *Clinical Chemistry* 46:593 [2000] Finding a needle in a haystack: detection and quantification of rare mutant alleles are coming of age.
- Ravine, *J Inherited Metab Dis* 22:503 [1999] Automated Mutation analysis.
- Hatch *et al.*, *Genet Anal* 15, 35-40. [1999] Rolling circle amplification of DNA immobilized on solid surfaces and its application to multiplex mutation detection. This reference is not being supplied at this time but will be supplied when available.

- Chen *et al.*, *Genome Res* 8, 549-56. A homogeneous, ligase-mediated DNA diagnostic test.
- Lizardi *et al.*, *Nat Genet* 19, 225-32. [1998] Mutation detection and single-molecule counting using isothermal rolling-circle amplification.
- Nilsson *et al.*, *Nat Genet* 16, 252-5. [1997] Padlock probes reveal single-nucleotide differences, parent of origin and in situ distribution of centromeric sequences in human chromosomes 13 and 21.
- Saiki *et al.*, *Science* 230, 1350-4. [1985] Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia.
- Stryer, *Annu Rev Biochem* 47, 819-46. [1978] Fluorescence energy transfer as a spectroscopic ruler. This reference is not being supplied at this time but will be supplied when available.
- Cardullo *et al.*, *Proc Natl Acad Sci U S A* 85, 8790-4. [1988] Detection of nucleic acid hybridization by nonradiative fluorescence resonance energy transfer.
- Ghosh *et al.*, *Nucleic Acids Res* 22, 3155-9. [1994] Real time kinetics of restriction endonuclease cleavage monitored by fluorescence resonance energy transfer.
- Chee *et al.*, *Science* 274, 610-4. [1996] Accessing genetic information with high-density DNA arrays.
- Shuber *et al.*, *Hum Mol Genet* 6, 337-47. [1997] High throughput parallel analysis of hundreds of patient samples for more than 100 mutations in multiple disease genes.
- Holland *et al.*, *Proc Natl Acad Sci U S A* 88, 7276-80. [1991] Detection of specific polymerase chain reaction product by utilizing the 5'----3' exonuclease activity of *Thermus aquaticus* DNA polymerase.
- Pastinen *et al.*, *Genome Res* 7, 606-14. [1997] Minisequencing: a specific tool for DNA analysis and diagnostics on oligonucleotide arrays.

- Wu *et al.*, *Proc Natl Acad Sci U S A* 86, 2757-60.[1989] Allele-specific enzymatic amplification of beta-globin genomic DNA for diagnosis of sickle cell anemia.
- Landegren *et al.*, *Science* 241, 1077-80. [1988] A ligase-mediated gene detection technique.
- Barany, *PCR Methods Appl* 1, 5-16. [1991] The ligase chain reaction in a PCR world.
- Barany, *Proc Natl Acad Sci U S A* 88, 189-93.[1991] Genetic disease detection and DNA amplification using cloned thermostable ligase.
- Landegren, U *et al.* *Genome Res* 8, 769-76. [1998] Reading bits of genetic information: methods for single-nucleotide polymorphism analysis.
- Schena, M. *et al.* *Trends Biotechnol* 16, 301-6. [1998] Microarrays: biotechnology's discovery platform for functional genomics.
- Gilles, P. N *et al.* *Nat Biotechnol* 17, 365-70. [1999] Single nucleotide polymorphic discrimination by an electronic dot blot assay on semiconductor microchips.
- Tang, K *et al.* *Proc Natl Acad Sci U S A* 96, 10016-20. [1999] Chip-based genotyping by mass spectrometry.
- Singh-Gasson, S. *et al.* *Nat Biotechnol* 17, 974-8. [1999] Maskless fabrication of light-directed oligonucleotide microarrays using a digital micromirror array.
- Cho, R. J. *et al.* *Nat Genet* 23, 203-7. [1999] Genome-wide mapping with biallelic markers in *Arabidopsis thaliana*.
- Hacia, J. G. *et al.* *Nat Genet* 22, 164-7. [1999] Determination of ancestral alleles for human single-nucleotide polymorphisms using high-density oligonucleotide arrays.
- Wang, D. G. *et al.* *Science* 280, 1077-82. [1998] Large-scale identification, mapping, and genotyping of single-nucleotide polymorphisms in the human genome.
- Hacia, J. G. *Nat Genet* 21, 42-7. [1999] Resequencing and mutational analysis using oligonucleotide microarrays. This reference is not being supplied at this time but will be supplied when available.



- Livak, K. *et al.*. *PCR Methods Appl* 4, 357-62. [1995] Oligonucleotides with fluorescent dyes at opposite ends provide a quenched probe system useful for detecting PCR product and nucleic acid hybridization.
- Tyagi, S *et al.*. *Nat Biotechnol* 16, 49-53. [1998] Multicolor molecular beacons for allele discrimination.
- Mutter, G. L., *et al.*. *Nucleic Acids Res* 23, 1411-8. [1995] PCR bias in amplification of androgen receptor alleles, a trinucleotide repeat marker used in clonality studies.
- Barnard, R. *et al.*. *Biotechniques* 25, 684-91. [1998] CR bias toward the wild-type k-ras and p53 sequences: implications for PCR detection of mutations and cancer diagnosis.
- Brookes, A. J. *Gene* 234, 177-86. [1999] The essence of SNPs.
- Lander, E. S. *Science* 274, 536-9. [1996] The new genomics: global views of biology.
- Hall, J. *et al.*. *Proc Natl Acad Sci U S A* 97, 8272-8277. [2000] From the cover: sensitive detection of DNA polymorphisms by the serial invasive signal amplification reaction.
- Hessner, M. J *et al.*. *Clin Chem* 46, 1051-6. [2000] Genotyping of factor V G1691A (Leiden) without the use of PCR by invasive cleavage of oligonucleotide probes.
- Ledford, M. *et al.*. *J Molec Diagnostics* 2, 97-104. [2000]. This reference is not being supplied at this time but will be supplied when available.
- Neri, B. P. *et al.*. in *Advances in Nucleic Acid and Protein Analysis* pp 117-125. [2000]. This reference is not being supplied at this time but will be supplied when available.
- Hall, J., *et al.*. *Hepatology* 28, 583A (abstract). [1998]
- Vener, T *et al.*. in *15<sup>th</sup> Ann Clin Vir Symp*, Clearwater Beach, FL. [1999]. This reference is not being supplied at this time but will be supplied when available.
- Lyamichev, V. *et al.*. *Nat Biotechnol* 17, 292-6. [1999] Polymorphism identification and quantitative detection of genomic DNA by invasive cleavage of oligonucleotide probes.

- Kwiatkowski, R. W *et al.*. *Mol Diagn* 4, 353-64. [1999] Clinical, genetic, and pharmacogenetic applications of the Invader assay.
- Reynaldo, L. P *et al.*. *J Mol Biol* 297, 511-20. [2000] The kinetics of oligonucleotide replacements.
- Lyamichev, V. I *et al.*. *Biochemistry* 39, 9523-32. [2000] Experimental and theoretical analysis of the invasive signal amplification reaction.
- Lyamichev, V.*et al.*. *Proc Natl Acad Sci U S A* 96, 6143-8. [1999] Comparison of the 5' nuclease activities of Taq DNA polymerase and its isolated nuclease domain.
- Hacia *et al.*. *J Med Genet* 36:730 [1999] Mutational analysis using oligonucleotide microarrays.
- Greer IA. *NEJM* 342:242 [2000] The challenge of thrombophilia in maternal-fetal medicine. This reference is not being supplied at this time but will be supplied when available.
- Gerhardt A *et al.*. *NEJM* 342:374 [2000] Prothrombin and factor V mutations in women with a history of thrombosis during pregnancy and the puerperium.
- Watkins H. *NEJM* 342:422 [2000] Sudden death in hypertrophic cardiomyopathy.
- Hillner B *Am J Hum Genet* 59:287 [1996] Genetic tests: a search for economy of scale.
- Wald NJ *et al.*. *BMJ* 319:1562 [1999] When can a risk factor be used as a worthwhile screening test?
- Jurkat-Rott, K *et al.*. *Nat Genet* 10, 111-3. [1995]
- La Du, B. N., *et al.*. *Cell Mol Neurobiol* 11, 79-89. [1991] Proposed nomenclature for human butyrylcholinesterase genetic variants identified by DNA sequencing.
- Kalow, W., and Grant, D. M. in *The metabolic and molecular bases of inherited disease* (Scriver, C. R., Stanbury, J. B., Wyngaarden, J. B., and Fredrickson, D. S., Eds.) pp 293-322, McGraw-Hill. [1995]. This reference is not being supplied at this time but will be supplied when available.

- Sachse, C. et al *N Engl J Med* 336, 399-403. [1997]. This reference is not being supplied at this time but will be supplied when available.
- De Stefano, V., et al.. *N Engl J Med* 341, 801-6. [1999] The risk of recurrent deep venous thrombosis among heterozygous carriers of both factor V Leiden and the G20210A prothrombin mutation.
- Majetschak, M., et al.. *Ann Surg* 230, 207-14.[1999] Relation of a TNF gene polymorphism to severe sepsis in trauma patients.
- Stuber, F. et al.. (1996) *Crit Care Med* 24, 381-4. A genomic polymorphism within the tumor necrosis factor locus influences plasma tumor necrosis factor-alpha concentrations and outcome of patients with severe sepsis. This reference is not being supplied at this time but will be supplied when available.
- Orkin, F., and Thomas, S. in *Anesthesia* (Miller, R., Ed.) pp 2579, Churchill Livingstone, Philadelphia, PA. [2000]
- Sindrup, S. H. et al. *Clin Pharmacol Ther* 48, 686-93. [1990] Codeine increases pain thresholds to copper vapor laser stimuli in extensive but not poor metabolizers of sparteine.
- Weisberg, I., et al. *Mol Genet Metab* 64, 169-72. [1998] A second genetic polymorphism in methylenetetrahydrofolate reductase (MTHFR) associated with decreased enzyme activity.
- Harmon, D. L et al..*Genet Epidemiol* 17, 298-309. [1999] Methionine synthase D919G polymorphism is a significant but modest determinant of circulating homocysteine concentrations.
- Tsai, M. Y. et al.. *Am J Hum Genet* 59, 1262-7.[1996] High prevalence of a mutation in the cystathionine beta-synthase gene.
- Brandt, A., et al.. *Hum Mol Genet* 8, 2055-62. [1999] Screening of the ryanodine receptor gene in 105 malignant hyperthermia families: novel mutations and concordance with the in vitro contracture test.
- Monnier, N et al.. *Am J Hum Genet* 60, 1316-25. [1997] Alignant-hyperthermia susceptibility is associated with a mutation of the alpha 1-subunit of the human dihydropyridine-sensitive L-type voltage-dependent calcium-channel receptor in skeletal muscle.

- Tarkowski, E *et al.*. *Neurology* 54, 2077-81. [2000] TNF gene polymorphism and its relation to intracerebral production of TNFalpha and TNFbeta in AD.
- Flach, R. *et al.*. *Cytokine* 11, 173-8. [1999] Relation of ex vivo stimulated blood cytokine synthesis to post-traumatic sepsis. This reference is not being supplied at this time but will be supplied when available.
- Mira, J. P. *et al.*. *JAMA* 282, 561-8. [1999] Association of TNF2, a TNF-alpha promoter polymorphism, with septic shock susceptibility and mortality: a multicenter study.
- Freeman, R. B *et al.*. *Transplantation* 67, 1005-10. [1999] Tumor necrosis factor genetic polymorphisms correlate with infections after liver transplantation. NEMC TNF Study Group. New England Medical Center Tumor Necrosis Factor.
- Faioni, E. M., *et al.*. *Blood* 94, 3062-6. [1999] Coinheritance of the HR2 haplotype in the factor V gene confers an increased risk of venous thromboembolism to carriers of factor V R506Q (factor V Leiden).
- Singer *et al.*. *BMJ* 319:501 [1999] ABC of intensive care. Cutting edge.
- Schroeder S *et al.*. *Crit Care Med* 27: 1265 [1999] Analysis of two human leukocyte antigen-linked polymorphic heat shock protein 70 genes in patients with severe sepsis.
- Wang AM *et al.*. *Science* 228:149 [1985] Molecular cloning of the complementary DNA for human tumor necrosis factor.
- Masterson GR/ *et al.*. *Br. J Anes* 77: 569 [1996] Does anaesthesia have long-term consequences?
- Kumar A *et al.*. *JAMA* 282;579 [1999] Genetic factors in septic shock.
- Carlsson LE *et al.*. *Blood* 92: 1526 [1998] Heparin-induced thrombocytopenia: new insights into the impact of the FcgammaRIIa-R-H131 polymorphism.
- Rieder MJ *et al.*. *Nature Genetics* 22:59 [1999] Sequence variation in the human angiotensin converting enzyme.
- Vaccarino V *et al.*. *Annals of Internal Medicine* 131:62 [1999] Risk factors for cardiovascular disease: one down, many more to evaluate.

- Schuckit MA. *JAMA* 281:1875 [1999] New findings in the genetics of alcoholism.
- Weiss EJ *et al.* *NEJM* 334:1090 [1996] A polymorphism of a platelet glycoprotein receptor as an inherited risk factor for coronary thrombosis.
- Goldschmidt-Clermont PJ. *et al.* *J Thromb and Thromb* 8:89 [1999] Platelet PLA2 polymorphism and thromboembolic events: from inherited risk to pharmacogenetics.
- Heron E. *et al.* *Arch Intern Med* 160:382 [2000] Hypercoagulable states in primary upper-extremity deep vein thrombosis.
- Gaughan G *et al.* *Genomics* 11:455 [1991] Refinement of the localization of human butyrylcholinesterase to chromosome 3q26.1-q26.2 using a PCR-derived probe.
- LaDu B *Acta Anaesthesiol Scand* 39:139 [1995] Butyrylcholinesterase variants and the new methods of molecular biology.
- Pantuck EJ *Anesth Analg* 77:380 [1993] Plasma cholinesterase: gene and variations.
- Jensen FS *et al.* *Acta Anaesthesiol Scand* 39:151 [1995] Plasma cholinesterase and abnormal reaction to succinylcholine: twenty years' experience with the Danish Cholinesterase Research Unit.
- Wood M *Anesthesiology* 71:631 [1989] Variability of human drug response.
- Johansson I *et al.* *PNAS* 90:11825 [1993] Inherited amplification of an active gene in the cytochrome P450 CYP2D locus as a cause of ultrarapid metabolism of debrisoquine.
- Kroemer HK *et al.* *Life Sciences* 56:2285 [1995] "It's the genes, stupid". Molecular bases and clinical consequences of genetic cytochrome P450 2D6 polymorphism.
- Nguyen A *Mayo Clin Proc* 75:595 [2000] Prothrombin G20210A polymorphism and thrombophilia.
- Poort SR *et al.* *Blood* 88:3698 [1996] A common genetic variation in the 3'-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis.

- Ridker PM *et al.* *Circulation* 99: 999 [1999] G20210A mutation in prothrombin gene and risk of myocardial infarction, stroke, and venous thrombosis in a large cohort of US men.
- Franco Rf *et al.* *Br J Haematology* 104:50 [1999] The 20210 G-->A mutation in the 3'-untranslated region of the prothrombin gene and the risk for arterial thrombotic disease.
- Griese EU *et al.* *Pharmacogenetics* 9:389 [1999] Detection of CYP2C19 alleles \*1, \*2 and \*3 by multiplex polymerase chain reaction.
- Morris P. *Pediatric Anaesthesia* 7:1 [1997] Duchenne muscular dystrophy: a challenge for the anaesthetist. This reference is not being supplied at this time but will be supplied when available.
- McNicholl JM *et al.* *Am J Prev Med* 16:141 [1999] Host genes and infectious diseases. HIV, other pathogens, and a public health perspective.
- Ulevitch RJ *Nature* 401:755 [1999] Toll gates for pathogen selection.
- Muzio M *et al.* *J Exp Med* 187:2097 [1998] The human toll signaling pathway: divergence of nuclear factor kappaB and JNK/SAPK activation upstream of tumor necrosis factor receptor-associated factor 6 (TRAF6).
- Sleight JW *Anaesth Int Care* 28:53 [2000]
- Hillier CEM. *et al.* *Q J Med* 91:677 [1998] Inherited prothrombotic risk factors and cerebral venous thrombosis.
- Bick RL *et al.* (eds.) *Sem in Thromb and Hemostasis* 25:251 [1999] Hereditary and acquired thrombophilia. Part I. Preface.
- Stratton MA *et al.* *Arch Int Med* 160:334 [2000] Prevention of venous thromboembolism: adherence to the 1995 American College of Chest Physicians consensus guidelines for surgical patients.
- Ginsberg JS *et al.* *Arch Int Med* 160:669 [2000] Postthrombotic syndrome after hip or knee arthroplasty: a cross-sectional study.
- Tardiff BE *et al.* *Ann Thorac Surg* 64:715 [1997] Preliminary report of a genetic basis for cognitive decline after cardiac operations. The Neurologic Outcome Research Group of the Duke Heart Center.

- Spiess BD *et al.*. *J Cardiothoracic and Vascular Anesthesia* 14:2 [2000]  
Overview of myocardial outcome: the interrelationships among coagulation, inflammation, and endothelium.
- Tam YK *Clin Pharmacokinetics* 25:300 [1993] Individual variation in first-pass metabolism.
- Nielsen EW *et al.*. *J Int Med* 239:119 [1996] Hereditary angio-oedema: new clinical observations and autoimmune screening, complement and kallikrein-kinin analyses. This reference is not being supplied at this time but will be supplied when available.
- Pastinen T *et al.*. *Hum Mol Gen* 7:1453 [1998] Array-based multiplex analysis of candidate genes reveals two independent and additive genetic risk factors for myocardial infarction in the Finnish population. This reference is not being supplied at this time but will be supplied when available.
- Drazen JM *et al.*. *Nature Genetics* 22: 168 [1999] Pharmacogenetic association between ALOX5 promoter genotype and the response to anti-asthma treatment.
- Ortega RA *et al.*. *Am J Anesth* Nov:429 [1999]
- Berkowitz DE *et al.*. *J Cardiothoracic and Vasc Anesth* 13:744 [1999]  
Molecular biology in cardiovascular anesthesiology: the brave new frontier.
- Ciccone GK *et al.*. *Br J Anaesth* 82:255 [1999] Drugs and sex differences: a review of drugs relating to anaesthesia.
- Martin G *et al.*. *Semin Anesth, Periop Med and Pain* 19: 76 [2000]
- Geelen JLM *Eur Heart J* 19:1427 [1998] Molecular genetics of inherited long QT syndromes.
- Priori S *et al.*. *Circulation* 99:529 [1999] Low penetrance in the long-QT syndrome: clinical impact.
- Bertholet M *et al.*. *Circulation* 99:1464 [1999] C-terminal HERG mutations: the role of hypokalemia and a KCNQ1-associated mutation in cardiac event occurrence.
- Busjahn A. *et al.*. *Circulation* 99:3161 [1999] QT interval is linked to 2 long-QT syndrome loci in normal subjects.

- Priori S *et al.*. *Circulation* 99:674 [1999] Genetic and molecular basis of cardiac arrhythmias: impact on clinical management part III.
- Pleym H *et al.*. *Acta Anaesth Scand* 43:352 [1999] Ventricular fibrillation related to reversal of the neuromuscular blockade in a patient with long QT syndrome.
- Priori S *et al.*. *Circulation* 99:518 [1999] Genetic and molecular basis of cardiac arrhythmias: impact on clinical management parts I and II.
- Graham RM *et al.* *NEJM* 341: 1759 [1999] Pathogenesis of inherited forms of dilated cardiomyopathy.
- Fananapazir L *JAMA* 281:1746 [1999] Advances in molecular genetics and management of hypertrophic cardiomyopathy.
- Bonne G *et al.*. *Circ Res* 83:580 [1998] Familial hypertrophic cardiomyopathy: from mutations to functional defects.
- Fuller BP *et al.*. *Science* 285:1359 [1999] Privacy in genetics research.
- Coughlin SS *Am J Prev Med* 16:89 [1999] The intersection of genetics, public health, and preventive medicine.
- Reid MC *et al.* *JAMA* 274:645 [1995] Use of methodological standards in diagnostic test research. Getting better but still not good.
- Holtzman NA *Science* 286:409 [1999] Are genetic tests adequately regulated?
- McGovern MM. *et al.* *JAMA* 281:835 [1999] Quality assurance in molecular genetic testing laboratories.
- Grody *et al.*. *JAMA* 281:845 [1999] Report card on molecular genetic testing: room for improvement?
- O'Donnell *et al.*, *NEJM* 342:240-245 [2000] Apolipoprotein E Genotype And The Risk Of Recurrent Labor Intracerebral Hemorrhage
- Caplan, *Anesthesia and Perioperative Complications*, second edition, [1999], pp. 760-770, The Cost of Adverse Outcome
- Posner *et al.*, *Anesthesia and Perioperative Complications*, second edition, [1999], pp. 752-759, Current Spectrum Of Anesthetic Injury.
- Lander, *Nature Genetics* [1999] 21:3-4, Array of Hope



- Southern *et al.*, *Nature Genetics* [1999] 21:5-8, Molecular Interactions on Microarrays
- Duggan *et al.*, *Nature Genetics* [1999] 21:10-14, Expression profiling using cDNA microarrays
- Cheung *et al.*, *Nature Genetics* [1999] 21:15-19, Making and reading microarrays
- Lipshutz *et al.*, *Nature Genetics* [1999] 21:20-24, High density synthetic oligonucleotide arrays
- Bowtell, *Nature Genetics* [1999] 21:25-32, Options available - from start to finish - for obtaining expression data by microarray
- Brown *et al.*, *Nature Genetics* [1999] 21:33-37, Exploring the new world of the genome with DNA microarrays
- Cole *et al.*, *Nature Genetics* [1999] 21:38-41, The genetics of cancer - a 3D model
- Debouck *et al.*, *Nature Genetics* [1999] 21:48-50, DNA microarrays in drug discovery and development
- Bassett *et al.*, *Nature Genetics* [1999] 21:51-55, Gene expression informatics it's all in your mine
- Chakravarti, *Nature Genetics* [1999] 21:56-60, Population genetics - making sense out of sequence
- The Blue Sheet, October 13, 1999
- Pharmacogenetics, Chapter 4, pp. 303-309
- Pharmacogenetics, Chapter 4, pp, 309-326
- Simioni *et al.*, *N. Engl. J. Med* [1997] 336:399-403, The risk of recurrent venous thromboembolism in patients with an Arg<sup>506</sup> →Gln mutation in the gene for factor V (factor V Leiden). This reference is not being supplied at this time but will be supplied when available.
- Lindmarker *et al.*, *Thromb Haemost* [1999] 81:684-9, The risk of recurrent venous thromboembolism in carriers and non-carriers of the G1691A allele in the coagulation factor V gene and the G20210A allele in the prothrombin gene. This reference is not being supplied at this time but will be supplied when available.

- Leroyer *et al.*, *Thromb Haemost* [1998] Prevalence of the 20210 A allele of the prothrombin gene in venous thromboembolism patients. This reference is not being supplied at this time but will be supplied when available.
- Margaglione *et al.*, *Ann Intern Med* [1998] 129:89-93 Increased risk for venous thrombosis in carriers of the prothrombin G→A<sup>20210</sup> gene variant. This reference is not being supplied at this time but will be supplied when available.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: March 28, 2001



David A. Casimir  
Registration No. 42,395  
MEDLEN & CARROLL, LLP  
220 Montgomery Street, Suite 2200  
San Francisco, California 94104  
415/705-8410